

Research Proposal: Early Integrated Supportive Care Study

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1. Summary

Currently at the BC Cancer Agency oncologists refer a patient to the Pain and Symptom Management/Palliative Care team (PSMPC) based on their practice. Their decisions are made subjectively and without standard guidelines/symptom assessment tools. Patients are sometimes referred quite late in their illness. The PSMPC team sees patients in their own clinic, separate from the oncologists, and do not often collaborate in a patient's care. Early integration of palliative care into oncological care has been shown to improve quality of life and to prolong survival, to reduce inappropriately aggressive oncological care at end of life, and to reduce costs of care. We are testing an earlier integrated oncology-palliative care model at the time of cancer diagnosis, with the aims of determining whether:

- 1) the introduction of PSMPC support at the time of diagnosis will lead to better symptom management and quality of life,
- 2) early integration of palliative care into medical oncology care will reduce aggressiveness of cancer treatment near end of life
- 3) a fully integrated service delivery model is sustainable.

Our model's intervention will provide for the early involvement of the PSMPC team in collaboration with the gastrointestinal (GI) oncology team in order to provide patients with support from both subspecialties at a single visit. Patients in need of pain and symptom support will be identified using a validated symptom assessment tool. The GI cancer team was approached for testing this model as their patients are referred more frequently to the PSMPC clinic in the Vancouver Centre than any other tumour site - 23.4% of total referrals. This intervention would be aimed particularly at helping the most unwell patients who find attendance at multiple appointments very difficult.

This study builds on work published in 2010 by Temel et al¹, which showed that early palliative care intervention improved the quality of life and survival time of metastatic lung cancer patients at the Massachusetts General Hospital, Boston. A 2014 study conducted by Bakitas et al in mixed cancers has shown similar benefits². Both these studies were in patients with advanced cancer and a short life expectancy. We propose to move the integration even earlier, to time of referral to oncology, to maximize the potential benefits. If the intervention is shown to benefit patients, we will have evidence to support the implementation of a new standard of cancer patient care.

2. Objectives

- A) To test whether the introduction of PSMPC support at a stage of patient care earlier than current practice (referral by the oncologist when deemed necessary) allows for better management of patients' pain and symptoms from cancer or its treatment, and improves quality of life of patients

- B) To test whether early integration of palliative care into medical oncology care reduces aggressiveness of cancer treatment near end of life
- C) To test whether a service delivery model in which PSMPC support is introduced at an early stage in patient care is sustainable

3. Intervention

The intervention is earlier PSMPC team involvement in patient care as informed by patients' self-reported symptom assessment.

Tool: symptom assessment questionnaire

Decision: patients with symptom scores ≥ 4 are identified as needing symptom management

Specialist involvement: patients in need will meet with a PSMPC team member either at the GI appointment (collaboration with GI team) or at a later date.

4. Assessment tool

Our patient assessment will be conducted using a modified BC Cancer Agency Patient Pain and Symptom Questionnaire, which includes the Edmonton Symptom Assessment Scale (ESAS) and the Canadian Problem Checklist (CPC). Our primary outcome of symptom assessment will be collected using the ESAS, which is a validated, reliable tool for patient symptom intensity³⁴. Several past palliative care studies have used the ESAS as an assessment tool, and have shown decreases in symptom scores following similar specialist team interventions⁵⁶⁷⁸.

5. Eligible patients

- diagnosed with a GI cancer (small intestine, colorectal, stomach*, esophageal*, pancreatic*, liver, gallbladder)
- have appointments in GI clinic during study days
- not yet receiving care from the PSMPC team
- can complete symptom assessment questionnaire on their own or with the help of a family member or interpreter

6. Study Design/Randomization

This is a cluster randomized study with the randomization being performed at the level of the oncologists. Controlled randomization allows us to make the intervention and control groups comparable with respect to all factors that could influence the outcome of the intervention.

Cluster randomization - oncologists will be randomized into either the intervention or the control group, and patients will be automatically sorted according to their oncologist's assigned group. By randomizing at the level of the oncologist and including multiple oncologists in each study arm, we can adjust for differences in schedules and referral patterns to ensure the groups are comparable.

Update 9-Feb-18:

All oncologists will be allocated to the intervention arm for the remainder of the study now that we have the desired sample size for the control group. By recording which oncologist saw which patient this will not be an issue for obtaining study outcomes.

7. Groups

Intervention

- *Assessment questionnaire + early PSMPC involvement*
- GI cancer patients complete a symptom assessment questionnaire prior to their oncology appointment.
- The questionnaire is reviewed and discussed with the oncologist.
- If a patient self-reports at least one symptom score ≥ 4 , the PSMPC team will be from the PSMPC clinic area to meet with the patient in the GI clinic, during or immediately following the oncology appointment.

Control

- *Assessment questionnaire for data collection only, not to be assessed*
- GI cancer patients will complete a symptom assessment questionnaire prior to their oncology appointment.
- The questionnaire data will not be shared with the oncologist. Control patients will be made aware that their questionnaire will not be discussed at this appointment, but that they are free to raise pain and symptom/palliative care concerns with the oncology team.
- Oncologists may refer patients to the PSMPC team if/when they deems necessary.

8. Sample Size

Our total estimated sample size is 176 and assumes a 5%* drop-out rate:

Integrated arm = 88

Control arm = 88

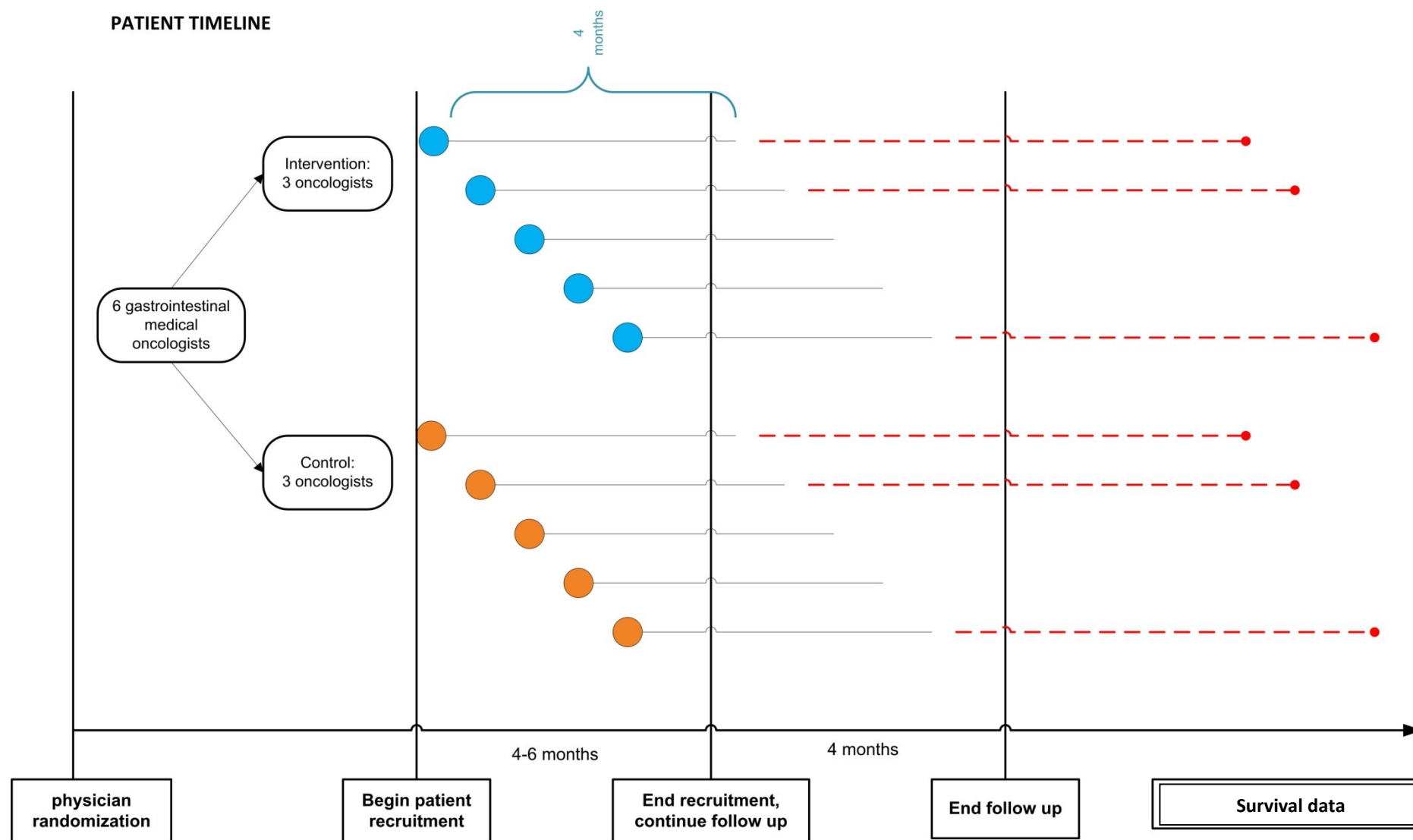
The sample size calculations were derived using Hemming et al⁹.

9. Patient recruitment

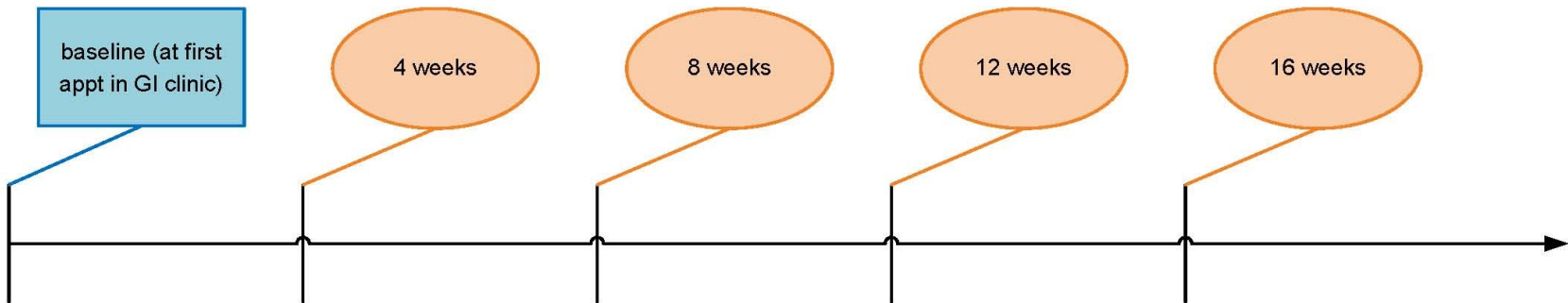
We will be recruiting new patients for a period of approximately 4-6 months. Based on the current new patient appointments, we estimate that for each study arm we can approach 17-20 patients a month on study days.

10. Patient following

Each patient will have data collected for four months.



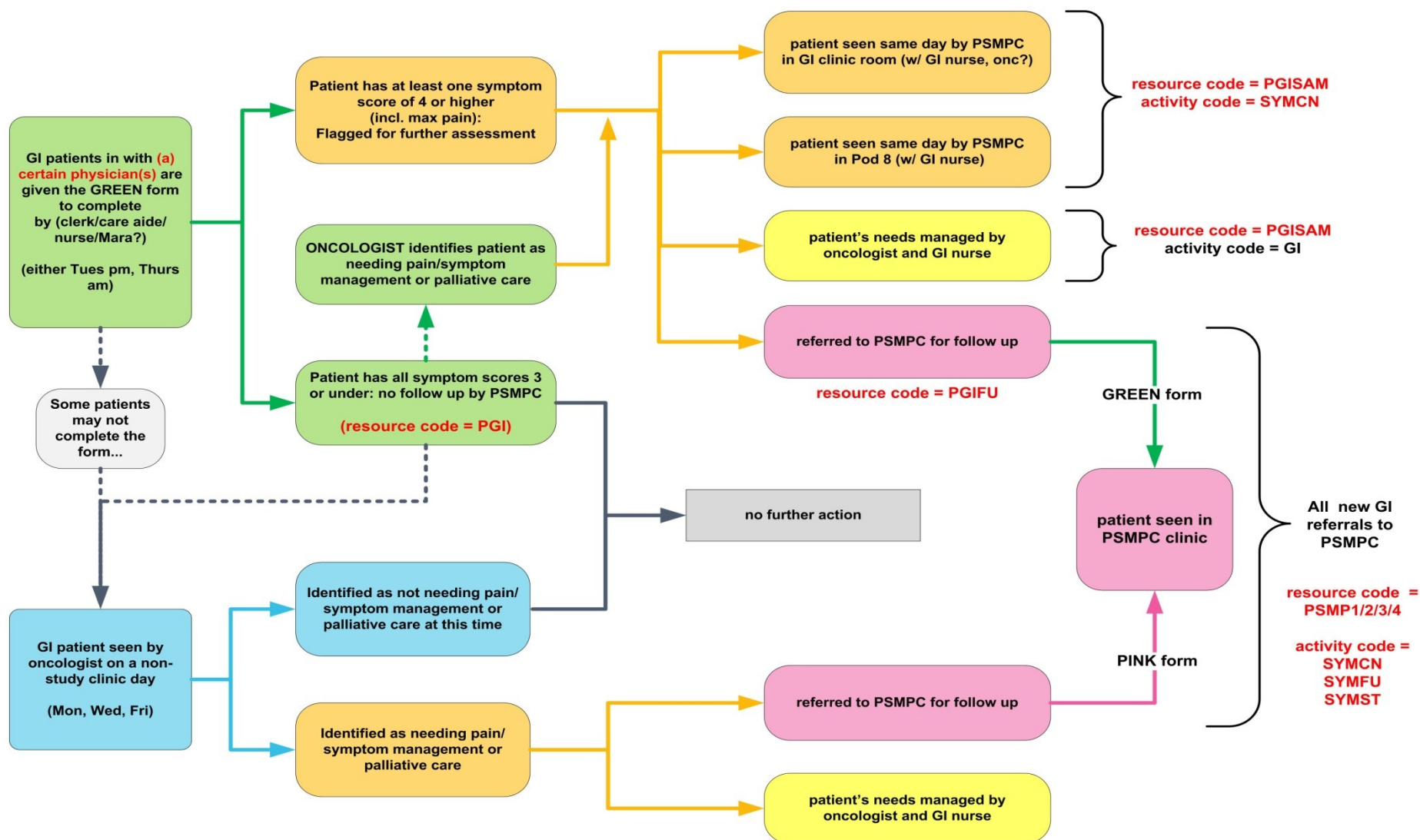
Timeline for collection of symptom assessment data (pink forms):
based on existing follow up schedule for patients

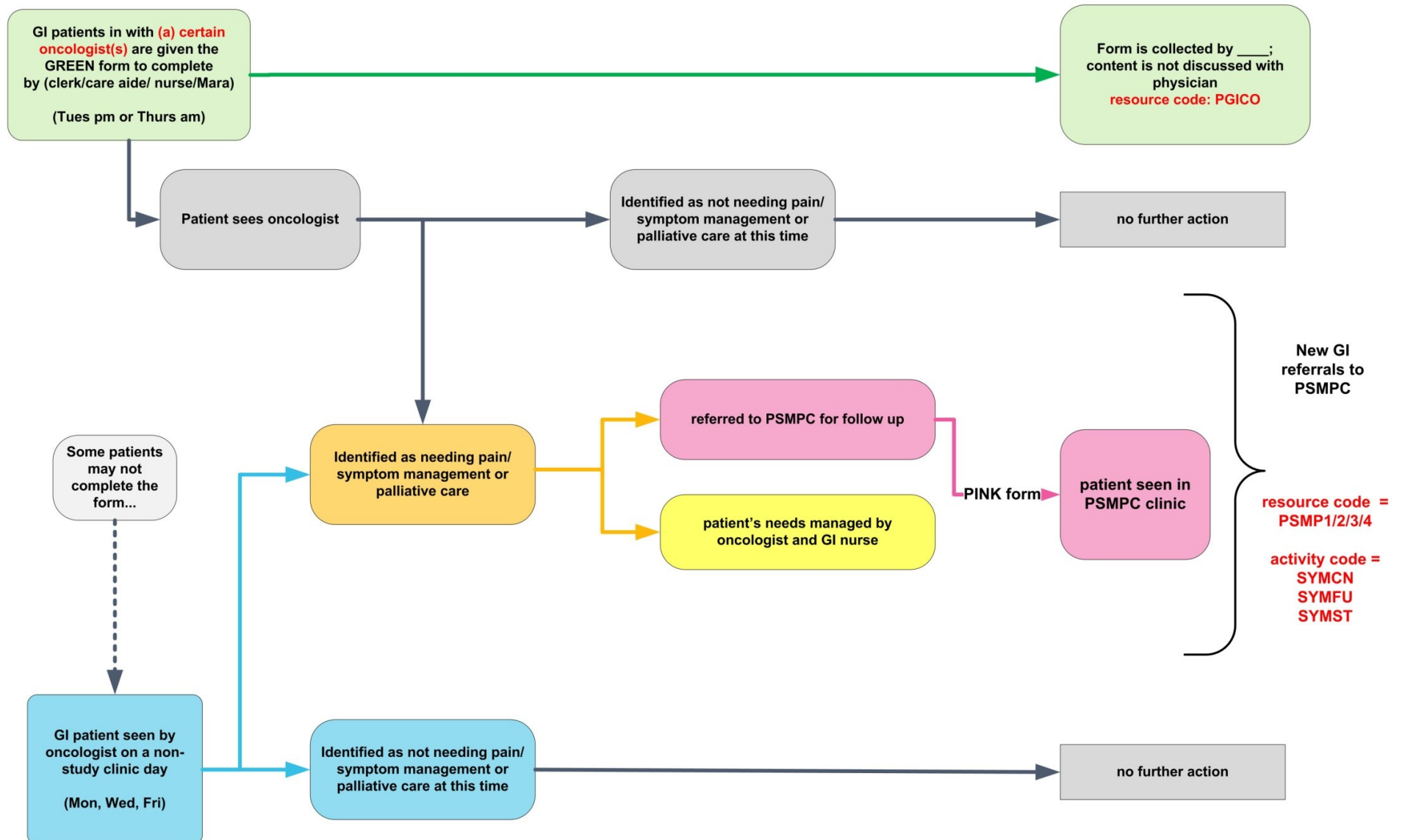


Intervention patients and control patients

11. Summary of Procedures

PC STUDY FLOW version B (grouped by physician) – intervention group





12. Outcome measures

Outcome category	Measure
Symptom assessment (aim: reduce symptoms)	Pain and symptom assessment questionnaire (ESAS) <ul style="list-style-type: none"> change in individual symptom scores between visits change in composite score of symptoms proportion with change in individual symptom scores of ≥ 2 points between first and last visits
Use of health services (aim: reduce incidence of non-treatment visits to hospital)	# of hospital admissions for non-treatment reasons
	# of ER visits
	# of referrals to PSMPC
	# of PSMPC follow up visits per patient
Aggressiveness of cancer treatment (aim: provide alternative to cancer treatment when no longer beneficial)	# of patients being treated with chemotherapy in last 2 - 4 weeks of life
	# of patients admitted to home hospice in last 3 days - 2 weeks of life
Details of death (aims: improve end of life care, improve survival time)	survival time (from first appointment at BC Cancer)
	location of death

Our primary outcome is the total distress score over time for each patient.

13. Estimated time frame

Activity	Length of time	Point in timeline
Patient recruitment and primary data collection	8-10 months	8-10 months
Survival follow up	12 months	20-22 months
Primary data analysis	2 months ?	22-24 months
study write up	4 months	26-28 months (2 years, 2-4 mon.)

14. Statistical Analysis

Our primary outcome is the total distress score over time for each patient. We will compare the individual distress scores within groups and between groups.

The intervention effect is expressed as the difference in mean changes in symptom scores from baseline to last follow-up between the two treatment groups. Our hypothesized effect size is 2 points. Based on previous studies^{7,10,11,12,13}, this difference is both realistic and clinically meaningful.

The type-1 error level and power of the study are pre-specified as 5% and 80%, respectively¹⁴.

The standard deviation is assumed to be the same in each treatment group (4 points), yielding a “medium” standardized effect size of $2 \text{ points} / 4 \text{ points} = 0.5$ ¹⁵.

The Intra-Cluster Correlation (ICC) coefficient, which represents how strongly patients within the same study group (cluster) are related to each other, is assumed to be $\rho = 0.005$ ¹⁶.

¹ Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, Dahlin CM, Blinderman CD, Jacobsen J, Pirl WF, Billings JA, Lynch TJ (2010) Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* Aug 19;363(8):733-42.

² Bakitas M, Doyle Lyons K, Hegel MT, Balan S, Brokaw FC, Seville J, Hull JG, Li Z, Tosteson TD, Byock IR, Ahles TA (2009) Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer (the Project ENABLE II randomized controlled trial). *JAMA* 302(7):741-49

³ Chang VT, Hwang SS, Meurerman M (2000) Validation of the Edmonton Symptom Assessment Scale. *Cancer* 88(9):2164-71.

⁴ Philip J, Smith WB, Craft P, Lickiss N (1998) Concurrent validity of the modified Edmonton Symptom Assessment System with the Rotterdam Symptom Checklist and the Brief Pain Inventory. *Support Care Cancer* 6:539-41

⁵ Bakitas M, Doyle Lyons K, Hegel MT, Balan S, Brokaw FC, Seville J, Hull JG, Li Z, Tosteson TD, Byock IR, Ahles TA (2009) Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer (the Project ENABLE II randomized controlled trial). *JAMA* 302(7):741-49

⁶ Bischoff K, Weinberg V, Rabow MW (2013) Palliative and oncologic co-management: symptom management for outpatients with cancer. *Support Care Cancer* 21:3031-37

⁷ Yennurajalingam S, Urbauer DL, Casper KLB, Reyes-Gibby CC, Chacko R, Poulter V, Bruera E (2011). Impact of a palliative care consultation team on cancer-related symptoms in advanced cancer patients referred to an outpatient supportive care clinic. *J Pain Sym Man* 41(1): 49-56

⁸ Zimmermann C, Swami N, Hannon B, Leigh N, Oza A, Moore M, Rydall A, Rodin G, Tannock I, Donner A, Lo C (2014) Early palliative care for patients with advanced cancer: a cluster-randomized controlled trial. *The Lancet* 383(9930):1721-1730.

⁹ Hemming K, Girling AJ, Sitch AJ, Marsh J, Lilford RJ (2011) Sample size calculations for cluster randomized controlled trials with a fixed number of clusters. *BMC Medical Research Methodology* 11:102 (<http://www.biomedcentral.com/content/pdf/1471-2288-11-102.pdf>)

¹⁰ Osoba D, Rodrigues G, Myles J, Zee B, Pater J (1998) Interpreting the significance of changes in health-related quality-of-life scores. *J Clin Oncol* 16:139-44

¹¹ Osoba D (2002) A taxonomy of the uses of health-related quality-of-life instruments in cancer care and the clinical meaningfulness of the results. *Med Care* 40:11131-38

¹² Barrett B, Brown D, Mundt M, Brown R (2005) Sufficiently important difference: expanding the framework of clinical significance. *Med Decis Making* 25:250-61

¹³ Ringash J, O'Sullivan B, Bezjak A, Redelmeier DA (2007) Interpreting clinically significant changes in patient reported outcomes. *Cancer* 110:196-202

¹⁴ Suresh KP and Chandrashekara S (2012) Sample size estimation and power analysis for clinical research studies. *J Hum Reprod Sci* 5(1): 7–13.

¹⁵ Book: "Statistical Power Analysis for the Behavioral Sciences", Second Edition, by Jacob Cohen, 1988 (Publisher: Lawrence Erlbaum Associates)

¹⁶ Bland JM (2004) Cluster randomised trials in the medical literature: two bibliometric surveys. *BMC Medical Research Methodology* 4, 21.